Amendments to the Claims

In accordance with 37 C.F.R. 1.173(b)(2), the following claims are changed or added by this amendment:

1. (Currently Amended; Amended Four Times) A method of locally administrating an active agent to a host, said method comprising:

retroinfusing said agent into a vascular vessel of said host under [conditions] pressure sufficient for a flowable formulation of said agent or a fluid delivery vehicle thereof to [produce a disruption in] disrupt a wall of said vessel wherein the integrity of the wall is compromised producing disruptive passageways there of and for said agent to enter an interstitial space of said host through said [disruption] disruptive passageways so that said agent is locally administered to said host.

2. (Original) The method according to claim 1, wherein said vessel is a vein.

3. (Previously Presented; Amended) The method according to claim 1, wherein said retroinfusing comprises providing stress to said vascular vessel at a site [at least] proximal to said interstitial space.

4. (Original) The method according to claim 1, wherein said method further comprises using depot means.

5. (Previously Presented; Amended) The method according to claim 1, wherein said method further comprises administration of energy to a wall of said vessel.

6. (Original) The method according to claim 1, wherein said interstitial space is myocardial interstitial space.

7. (Previously Presented; Amended) The method according to claim 3, wherein said retroinfusing comprises administering said agent in a flowable formulation at a pressure sufficient to produce [at least] a mechanical stress on a wall of said vessel.

8. (Currently Amended; Amended Four Times) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vein of said host under conditions sufficient for a flowable formulation of said agent or a fluid delivery vehicle thereof to [produce a disruption in] mechanically stress a wall of said vein [vessel] to disrupt the wall wherein the integrity of the wall is compromised producing disruptive passageways thereof and for said agent to enter an interstitial space of said host through said [disruption]disruptive passageways so that said agent is locally administered to said host.

9. (Currently Amended; Twice Amended) The method according to claim 8, wherein said retroinfusing comprises administering said agent in a flowable formulation at a pressure sufficient to produce [at least a] the mechanical stress on the wall of said vessel.

10. (Original) The method according to claim 8, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

11. (Previously Presented; Twice Amended) The method according to claim 8, wherein said method further comprises producing [inflamation] inflammation in a wall of said vein.

12. (Original) The method according to claim 8, wherein said interstitial space is myocardial interstitial space.

13. (Previously Presented; Amended) The method according to claim 9, wherein said pressure is sufficient to [at least] distend and disrupt a wall of said vein.

14. (Previously Presented; Amended) The method according to claim 9, wherein said pressure is sufficient to disrupt a wall of said vein.

15. (Previously Presented; Thrice Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vein of said host with a catheter and at a pressure sufficient for a flowable formulation of said agent or a fluid delivery vehicle thereof to produce a disruption [[on]] in a wall of said vein wherein the integrity of the wall is

compromised producing a disruptive passageway through the wall of said vein such that said agent enters an interstitial space proximal to the vein through said [disruption]disruptive passageway in the wall of said vein;

whereby said agent is locally administered to said host.

16. (Previously Presented; Amended) The method according to claim 15, wherein said pressure is sufficient to [at least] distend and disrupt a wall of said vein.

17. (Currently Amended; Twice Amended) The method according to claim [[16]]15, wherein said pressure is sufficient to disrupt a wall of said vein.

18. (Original) The method according to claim 16, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

19. (Previously Presented; Twice Amended) The method according to claim 16, wherein said method further comprises producing [inflamation] inflammation in a wall of said vein.

20. (Previously Presented) The method of claim 1 wherein said agent comprises cells.

21. (Previously Presented) The method of claim 1 wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

22. (Previously Presented) The method of claim 1 wherein said agent comprises therapeutic nucleic acids.

23. (Previously Presented) The method of claim 22 wherein the therapeutic nucleic acids comprise at least one gene.

24. (Previously Presented) The method of claim 1 wherein said agent comprises a dye or an imaging agent.

25. (Previously Presented) The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 50 mm Hg.

26. (Previously Presented) The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 60 mm Hg.

27. (Previously Presented) The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 1000 mm Hg.

28. (Previously Presented) The method of claim 5 wherein the energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

29. (Previously Presented; Amended) The method of claim 3 wherein said stress includes chemical stress.

30. (Previously Presented) The method of claim 1 wherein said vessel is an artery.

31. (Previously Presented; Amended) The method of claim 2 wherein said retroinfusion comprises disrupting venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptive passageways in the venous branches.

32. (Currently Amended; Amended) The method of claim 1 wherein said agent is retroinfused through a catheter having an occlusion device to occlude the vessel downstream of the site of administration of said agent.

33. (Previously Presented) The method of claim 32 wherein at least one upstream branch of said vessel is occluded.

34. (Previously Presented) The method of claim 2 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

35. (Previously Presented; Amended) The method of claim 34 wherein said retroinfusion comprises disrupting venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptive passageways in the venous branches.

36. (Previously Presented; Amended) The method of claim 1 wherein said pressure is sufficient to distend and disrupt a wall of said vessel.

37. (Currently Amended; Amended Four Times) A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid comprising the agent into a vascular vessel of said host under conditions sufficient for the fluid to mechanically stress a wall of said vessel to disrupt the wall wherein the integrity of the wall is compromised forming disruptive passageways thereof and infusing said agent into an interstitial space of said host through said disruptive passageways and locally administering said agent to said host through said disruptive passageways.

38. (Previously Presented) The method according to claim 37, wherein said vessel is a vein.

39. (Previously Presented; Amended) The method according to claim 37, wherein said retroinfusing comprises providing stress to a wall of said vascular vessel at a site proximal to said interstitial space.

40. (Previously Presented) The method according to claim 37, wherein said method further comprises using depot means.

41. (Previously Presented; Amended) The method according to claim 37, wherein said method further comprises administration of energy to a wall of said vessel.

42. (Previously Presented) The method according to claim 37, wherein said interstitial space is myocardial interstitial space.

43. (Previously Presented; Amended) The method according to claim 39, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce a mechanical stress in a wall of said vessel.

44. (Previously Presented; Thrice Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vein of said host under pressure sufficient for the fluid to disrupt a wall of said vein wherein the integrity of the wall is compromised creating a disruptive passageway through said wall and infusing said agent into an interstitial space of said host through said disruptive passageway so that said agent is locally administered to said host.

45. (Previously Presented; Amended) The method according to claim 44, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce a mechanical stress in a wall of said vein.

46. (Previously Presented) The method according to claim 44, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

47. (Previously Presented; Amended) The method according to claim 44, wherein said method further comprises producing inflammation in a wall of said vein.

48. (Previously Presented) The method according to claim 44, wherein said interstitial space is myocardial interstitial space.

49. (Previously Presented; Amended) The method according to claim 45, wherein said pressure is sufficient to distend and disrupt a wall of said vein.

50. (Previously Presented; Amended) The method according to claim 45, wherein said pressure is sufficient to disrupt a wall of said vein.

51. (Previously Presented; Thrice Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vein of said host with a catheter and at a pressure sufficient for the fluid to compromise the integrity of a wall of said vein and produce disruptive passageways in the wall of said vein and infusing said agent into an interstitial space proximal to the vein through said disruptive passageways;

whereby said agent is locally administered to said host.

52. (Previously Presented; Amended) The method according to claim 51, wherein said pressure is sufficient to distend and disrupt a wall of said vein.

53. (Currently Amended; Twice Amended) The method according to claim 51, wherein said pressure is sufficient to disrupt a wall of said vein.

54. (Previously Presented) The method according to claim 52, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

55. (Previously Presented; Amended) The method according to claim 52, wherein said method further comprises producing inflammation in a wall of said vein.

56. (Previously Presented; Thrice Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vascular vessel of said host under conditions sufficient for a flowable formulation of said agent or a fluid delivery vehicle thereof to produce a mechanical stress on a wall of said vessel, which stress facilitates the disruption of said wall wherein the integrity of the wall is compromised creating disruptive passageways there through and transport of said agent through said disruptive passageways in said wall of said vessel so that said agent is locally administered to said host,

wherein said method further comprises administration of energy to a wall of said vessel.

57. (Previously Presented; Twice Amended) The method according to claim 56, wherein said retroinfusing comprises administering the agent or the fluid delivery vehicle thereof at a pressure sufficient to distend and disrupt a wall of said vessel.

58. (Previously Presented; Twice Amended) The method according to claim 56, wherein said retroinfusing comprises administering the agent or the fluid delivery vehicle thereof at a pressure sufficient to disrupt a wall of said vessel.

59. (Previously Presented) The method according to claim 56, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

60. (Previously Presented; Amended) The method according to claim 56, wherein said method further comprises producing inflammation in a wall of said vessel.

61. (Previously Presented) The method of claim 56 wherein said vessel is an artery.

62. (Previously Presented; Amended) The method of claim 58 wherein said vessel is a vein, and said retroinfusion comprises disrupting venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through disruptive passageways in the venous branches.

63. (Currently Amended; Amended) The method of claim 56 wherein said agent is retroinfused through a catheter having an occlusion device to occlude the vessel downstream of the site of administration of said agent.

64. (Previously Presented) The method of claim 63 wherein at least one upstream branch of said vessel is occluded.

65. (Currently Amended; Amended) The method of claim 58 wherein said agent is retroinfused through a catheter having an occlusion device to occlude the vessel downstream of the site of administration of said agent.

66. (Previously Presented) The method of claim 65 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

67. (Currently Amended; Amended Four Times) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vascular vessel of said host under conditions sufficient for a flowable formulation of the agent or a fluid delivery vehicle thereof to distend a wall of said vessel, which distention leads to the disruption of said wall wherein the integrity of the wall is compromised creating disruptive passageways thereof and the transport of said agent through the disruptive passageways in said wall of said vessel so that said agent is locally administered,

wherein said method further comprises administration of energy to said wall of said vessel.

68. (Previously Presented; Amended) The method according to claim 67, wherein said retrofusing comprises administering said fluid at a pressure sufficient to produce a mechanical stress on said vessel.

69. (Previously Presented; Twice Amended) The method according to claim 67, wherein said retroinfusing comprises administering the flowable formulation of the agent or the fluid delivery vehicle thereof at a pressure sufficient to disrupt said vessel.

70. (Previously Presented) The method according to claim 67, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

71. (Previously Presented; Amended) The method according to claim 67, wherein said method further comprises producing inflammation in a wall of said vessel.

72. (Previously Presented) The method of claim 67 wherein said vessel is an artery.

73. (Previously Presented; Amended) The method of claim 69 wherein said vessel is a vein, and wherein said retroinfusion comprises disrupting venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through disruptive passageways in the venous branches.

74. (Currently Amended; Amended) The method of claim 67 wherein said agent is retroinfused through a catheter having an occlusion device to occlude the vessel downstream of the site of administration of said agent.

75. (Previously Presented) The method of claim 74 wherein at least one upstream branch of said vessel is occluded.

76. (Currently Amended; Amended) The method of claim 69, wherein said agent is retroinfused through a catheter having an occlusion device to occlude the vessel downstream of the site of administration of said agent.

77. (Previously Presented; Amended) The method of claim 76, wherein said vessel is a vein, and wherein said retroinfusion comprises disrupting venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through disruptive passageways in the venous branches.

78. (Currently Amended; Amended Four Times) A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid comprising the agent into a vascular vessel of said host under conditions sufficient for the fluid to produce a mechanical stress in said vessel, which stress facilitates the disruption of said wall wherein the integrity of the wall is compromised

creating disruptive passageways thereof and transport of said agent through said disruptive passageways in said wall of said vessel so that said agent is locally administered to said host,

wherein said method further comprises administration of energy to said vessel.

79. (Previously Presented) The method according to claim 78, wherein said vessel is a vein.

80. (Previously Presented; Twice Amended) The method according to claim 78, wherein said retroinfusing comprises administering the fluid at a pressure sufficient to distend and disrupt a wall of said vessel.

81. (Previously Presented; Twice Amended) The method according to claim 78, wherein said retroinfusing comprises administering the fluid at a pressure sufficient to disrupt a wall of said vessel.

82. (Previously Presented) The method according to claim 78, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

83. (Previously Presented; Amended) The method according to claim 78, wherein said method further comprises producing inflammation in a wall of said vessel.

84. (Previously Presented) The method of claim 78 wherein said vessel is an artery.

85. (Previously Presented; Amended) The method of claim 78 wherein said vessel is a vein, and said retroinfusion comprises disrupting venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through disruptive passageways in the venous branches.

86. (Currently Amended; Amended) The method of claim 78 wherein said agent is retroinfused through a catheter having an occlusion device to occlude the vessel downstream of the site of administration of said agent.

87. (Previously Presented) The method of claim 86 wherein at least one upstream branch of said vessel is occluded.

88. (Currently Amended; Amended) The method of claim 81 wherein said agent is retroinfused through a catheter having an occlusion device to occlude the vessel downstream of the site of administration of said agent.

89. (Previously Presented; Amended) The method of claim 88 wherein said vessel is a vein, and said retroinfusion comprises disrupting venous branches upstream of

the site of administration for said agent to enter an interstitial space of said host through the disruptive passageways in the venous branches.

90. (Currently Amended; Amended Four Times) A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vascular vessel of said host under conditions sufficient for the fluid to at least distend said vessel, which distention leads to the disruption of said wall wherein the integrity of the wall is compromised creating disruptive passageways thereof and transport of said agent through said disruptive passageways in said wall of said vessel so that said agent is locally administered to said host,

wherein said method further comprises administration of energy to said vessel.

91. (Previously Presented) The method according to claim 90, wherein said vessel is a vein.

92. (Previously Presented; Twice Amended) The method according to claim 90, wherein said retroinfusing comprises administering the fluid at a pressure sufficient to disrupt a wall of said vessel.

93. (Previously Presented) The method according to claim 90, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

94. (Previously Presented; Amended) The method according to claim 90, wherein said method further comprises producing inflammation in a wall of said vessel.

95. (Previously Presented) The method of claim 90 wherein said vessel is an artery.

96. (Previously Presented; Twice Amended) The method of claim 92 wherein said vessel is a vein, and said retroinfusion comprises disrupting venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptive passageways in the venous branches.

97. (Currently Amended; Amended) The method of claim 90 wherein said agent is retroinfused through a catheter having an occlusion device to occlude the vessel downstream of the site of administration of said agent.

98. (Previously Presented) The method of claim 97 wherein at least one upstream branch of said vessel is occluded.

99. (Currently Amended; Amended) The method of claim 92, wherein said agent is retroinfused through a catheter having an occlusion device to occlude the vessel downstream of the site of administration of said agent.

100. (Previously Presented; Amended) The method of claim 99, wherein said vessel is a vein, and wherein said retroinfusion comprises disrupting venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptive passageways in the venous branches.

101. (Previously Presented) The method according to claim 56, wherein said energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

102. (Previously Presented) The method according to claim 67, wherein said energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

103. (Previously Presented) The method according to claim 78, wherein said energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

104. (Previously Presented) The method according to claim 90, wherein said energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.